

THE MERCK INDEX

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CHEMICALS AND DRUGS

NINTH EDITION

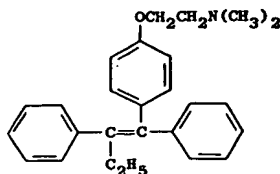
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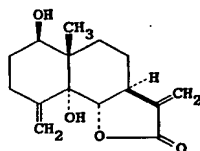
EXHIBIT A

ration of isomers: Bedford, Richardson, *Nature* 212, 733 (1966); Harper *et al.*, Brit. pat. 1,064,629; Fr. Addn. pat. 90,418 (both 1967 to I.C.I.). Comparative activity of isomers: Harper, Walpole, *Nature* 212, 87 (1966). Pharmacology: *eidem*, *J. Endocrinol.* 37, 83 (1967); *J. Reprod. Fert.* 13, 101 (1967); Terenius, *Acta Endocrinol. (Copenhagen)* 64, 47 (1970).



Crystals from petr ether, mp 96-98°. Citrate, $C_{21}H_{27}NO_{10}$, ICI-46474, Nolvadex, mp 140-142°. *cis*-Form base, mp 72-74° from methanol. *cis*-Form citrate, $C_{21}H_{27}NO_{10}$, ICI-47699, mp 126-128°. THERAP CAT: Anti-estrogen.

8824. Tanacetin. Decahydro-6 β ,9 α -dihydroxy-5 α -methyl-3,9-bis(methylene)naphthof[1,2-b]furan-2(3H)-one; 1 β ,5 α -dihydroxy-6 β ,7 α -H-selina-4(15),11(13)-dien-6,12-olide. $C_{21}H_{27}O_5$, mol wt 264.31. C 68.16%, H 7.63%, O 24.21%. Isolin from seed, herb, and flowers of *Tanacetum vulgare* L., Compositae: Homolle, *J. Pharm. Chim.* 7, 57 (1845); Jaretsky, Kühne, *Arch. Pharm.* 271, 353 (1933); Suchy, *Coll. Czech. Chem. Commun.* 27, 1058 (1962). Structure and absolute config: Samek *et al.*, *ibid.* 38, 1971 (1973).



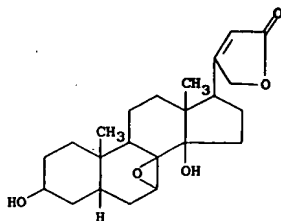
Crystals, mp 205°. $[\alpha]_D^{25} + 179.5^\circ$ ($c = 2.3$ in ethanol).

8825. Tanganil. *N*-Acetyl-leucine compound with 2-aminoethanol; monoethanolamine DL-acetyl-leucinate; DL-acetyl-leucine monoethanolamine salt; monoethanolamine salt of α -acetamidoisocaproic acid; RP 7452. $C_{10}H_{21}N_2O_6$, mol wt 234.29. C 51.26%, H 9.46%, N 11.96%, O 27.32%. Prepn: Gailliot *et al.*, U.S. pat. 2,941,924 (1960 to Rhône-Poulenc).



Crystals, mp about 150°. Soly in water: >20%; slight soly in alcohol: ~1%. pH of 10% aq soln: about 6. THERAP CAT: Antivertigo agent.

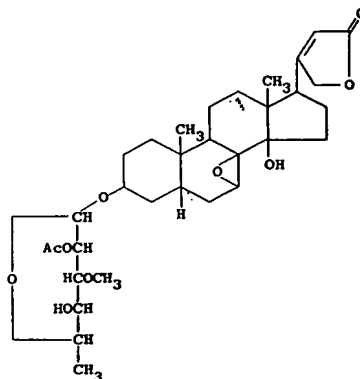
8826. Tanghinigenin. 7 β ,8-Epoxy-3 β ,14-dihydroxy-5 β -card-20(22)-enolide. $C_{31}H_{42}O_5$, mol wt 388.49. C 71.10%, H 8.30%, O 20.59%. Isolin from glucosides: Sigg *et al.*, *Helv. Chim. Acta* 38, 166 (1955). Structure: Flury, Reichstein, *Ann. Chim. (Rome)* 53, 23 (1963); Flury *et al.*, *Helv. Chim. Acta* 48, 1113 (1965).



Prisms from acetone + petr ether, mp 187-188°. $[\alpha]_D^{25} + 14.1^\circ$ ($c = 1.138$ in chloroform). uv max: 217 nm ($\log \epsilon$ 4.22). LD₅₀ in cats: 1 mg/kg i.v., Chen, Henderson, *J. Pharmacol. Exp. Ther.* 111, 365 (1954).

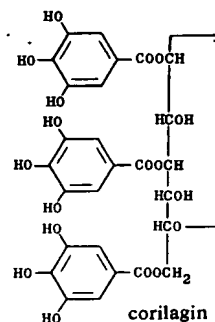
Acetate, $C_{33}H_{44}O_6$, acetyltanghinigenin. Prisms from acetone + petr ether, mp 241-243°. $[\alpha]_D^{25} + 14.9^\circ$ ($c = 1.075$ in chloroform).

8827. Tanghinin. 3 β -[(2-O-Acetyl-6-deoxy-3-O-methyl- α -L-glucopyranosyl)oxy]-7 β ,8-epoxy-14-hydroxy-5 β -card-20(22)-enolide. $C_{31}H_{46}O_{10}$, mol wt 590.69. C 65.06%, H 7.85%, O 27.09%. From the seed of *Tanghinia madagascariensis* Pet., Apocynaceae and *Tanghinia venenifera* Poir., Apocynaceae. Isolin: Arnaud, *Compt. Rend.* 108, 1255 (1889); Frèrejacque *et al.*, *ibid.* 226, 268 (1948). Tentative structure: Sigg *et al.*, *Helv. Chim. Acta* 38, 166 (1955). Revised structure: Flury, Reichstein, *Ann. Chim. (Rome)* 53, 23 (1963).



Leaflets from methanol + ether, mp 128-131°. $[\alpha]_D^{25} - 81.5^\circ$ ($c = 1.092$ in methanol). uv spectra: Frèrejacque *et al.*, *Helv. Chim. Acta* 39, 1900 (1956). LD₅₀ in cats: 0.4 mg/kg i.v., Chen, Henderson, *J. Pharmacol. Exp. Ther.* 111, 365 (1954).

8828. Tannic Acid. Tannin; gallotannin; gallotannic acid. Incorrectly "digallic acid". Tannic acid of commerce usually contains about 10% H₂O. Occurs in the bark and fruit of many plants, notably in the bark of the oak species, in sumac and myrobalan. It is produced from Turkish or Chinese nutgall, the former contg 50-60%, the latter about 70%. The chemistry of the tannins is most complex and non-uniform. Tannins may be divided into 2 groups: (a) derivatives of flavanols, so-called condensed tannins and (b) hydrolyzable tannins (the more important group) which are esters of a sugar, usually glucose, with one or more trihydroxybenzenecarboxylic acids. The structure given here is that of a tannin named corilagin: Schmidt *et al.*, *Ann.* 587, 67 (1954). The empirical formula of corilagin is $C_{27}H_{24}O_{18}$. For the commercial tannic acid, whose specifications follow, the empirical formula is usually given as $C_{16}H_{12}O_{10}$. Comprehensive reviews: M. Nierenstein, *The Natural Organic Tan-*



nins (London, 1934); O. Th. Schmidt, "Gallotannine" in *Fortschr. Chem. Org. Naturst.* 13, 70-136 (1956); *Symposium on the Chemistry of Vegetable Tannins* (Soc. Leather Trades Chemists, Croydon 1956).

Yellowish-white to light brown, amorphous, bulky powder or flakes, or spongy masses; faint characteristic odor; astringent taste. Gradually darkens on exposure to air and light; at 210-215° dec mostly into pyrogallol and CO₂. Gives insol ppts with albumin, starch, gelatin, most alkaloidal and metallic salts; produces a bluish-black color or precip with ferric salts. One gram dissolves in 0.35 ml water, 1 ml warm glycerol; very sol in alc, acetone; practically insol in benzene, chloroform, ether, petr ether, carbon disulfide, carbon tetrachloride. *Keep well closed and protected from light.* LD₅₀ orally in mice: 6.0 g/kg. Robinson, Graessle, *J. Pharmacol. Exp. Ther.* 77, 63 (1943).

Incompat: Salts of heavy metals, alkaloids, gelatin, albumin, starch, oxidizing substances—e.g., permanganates, chlorates; spirit nitrous ether, lime water.

USE: Mordant in dyeing; manuf ink; sizing paper and silk; printing fabrics; with gelatin and albumin for manuf of imitation horn and tortoise shell; tanning; clarifying beer or wine; in photography; as coagulant in rubber manuf; manuf gallic acid and pyrogallol; as reagent in analytical chemistry.

THERAP CAT: Astringent.

THERAP CAT (VET): Astringent, hemostatic, in solutions for burns. Has been used internally as an astringent and as a heavy metal antidote.

8829. Tannoforn. *Methyleneditannin*; tannin-formaldehyde; Helgotan. Prep'd by condensing one mole formaldehyde with two moles tannin: Chemnitz, *Pharm. Zentralh.* 68, 273 (1927); Schwyzer, *Pharm. Ztg.* 74, 1334 (1929).

Reddish, odorless, tasteless, bulky powder, mp about 230° with decompn. Practically insol in water; sol in alcohol, alkaline fluids.

THERAP CAT: Astringent.

THERAP CAT (VET): Externally as astringent, antiseptic (skin lesions and otorrhea). Has been used internally for diarrhea.

8830. Tanphetamin. *d*-Amphetamine tannate; Synatan. A 17.5 mg dose is equivalent to 4.98 mg of *d*-amphetamine base. Prep'd by the reaction of *d*-amphetamine (free base) with tannic acid in isopropanol: Cavallito, U.S. pat. 2,950,309 (1960 to Irwin, Neisler and Co.).

Caution: Excessive use may lead to tolerance and physical dependence.

THERAP CAT: Adrenergic.

8831. Tantalum. Ta; at. wt 180.9479; at. no. 73; valence 5, also 4, 3, 2. Two naturally occurring isotopes: 181 (99.9877%); 180 (0.0123%); $T_{1/2} > 10^{12}$ years; artificial radioactive isotopes: 172-179; 182-186. Occurs almost invariably with niobium; less abundant than niobium. Found in the minerals columbite (*q.v.*), *tantalite* [(Fe,Mn)(Ta,Nb)₂O₆] and *microlite* [(Na,Ca)₂Ta₂O₆(OH,F)]. Discovered by Ekeberg in 1802; first obtained pure by Bolton: *Z. Elektrochem.* 11, 45 (1905). Prep'n: Schoeller, Powell, *J. Chem. Soc.* 119, 1927 (1921). Reviews of tantalum and its compounds: G. L. Miller, *Tantalum and Niobium* (Academic Press, New York, 1959) 767 pp; Brown, "The Chemistry of Niobium and Tantalum" in *Comprehensive Inorganic Chemistry* vol. 3, J. C. Bailar, Jr. et al., Eds. (Pergamon Press, Oxford, 1973) pp 553-622.

Gray, very hard, malleable, ductile metal; can readily be drawn in fine wires. mp 2996°. bp 5429°. d 16.69. Spec heat (0°): 0.036 cal/g/°C. Electrical resistivity (18°): 12.4 μhm-cm. Insol in water. Very resistant to chemical attack; not attacked by acids other than hydrofluoric; not attacked by alkalis; slowly attacked by fused alkalis. Reacts with fluorine, chlorine, and oxygen only on heating. At high temps absorbs several hundred times its volume of hydrogen; combines with nitrogen, with carbon.

USE: In pen points; analytical weights; apparatus and instruments for chemical, surgical, and dental use instead of platinum, in tantalum capacitors (a type of electrolytic condenser, trademarked "Tantalytic").

THERAP CAT: Surgical aid.

8832. Tantalum Pentachloride. Cl₅Ta; mol wt 358.24. Cl 49.50%, Ta 50.50%. TaCl₅. Prep'n: Rolsten, *J. Am.*

Chem. Soc. 80, 2952 (1958). Review of tantalum halides: Fairbrother in *Halogen Chemistry* vol. 3, V. Gutmann, Ed. (Academic Press, New York, 1967) pp 123-178.

White or light yellow, cryst powder; monoclinic; dec in moist air. d 3.68; mp 216.5-220°. Begins to volatilize at 144°, bp 239.3°. Dec by water; sol in abs alcohol. LD₅₀ orally in rats: 1.9 g/kg.

8833. Tantalum Pentafluoride. F₅Ta; mol wt 275.95, F 34.43%, Ta 65.57%. TaF₅. Prep'd from tantalum pentachloride by the halide exchange method according to the equation TaCl₅ + 5HF → TaF₅ + 5HCl: Ruff, Zedner, *Ber.* 42, 492 (1909); Ruff, Schiller, *Z. Anorg. Allgem. Chem.* 72, 329 (1911); Kwasnik in *Handbook of Preparative Inorganic Chemistry* vol. 1, G. Brauer, Ed. (Academic Press, New York, 2nd ed, 1963) pp 255-256. Prep'n from the elements: Fairbrother, Frith, *J. Chem. Soc.* 1951, 3051. Review of transition metal pentafluorides: Peacock, *Advan. Fluoride Chem.* 7, 113-145 (1973).

Deliquescent, strongly refractive prisms. d₂₀ 4.74, mp 96.8°. Also reported as 95.1°: Fairbrother, Frith, *loc. cit.* bp 229.5°. Sol in water and ether with formation of oxyfluoro complexes. Also sol in concd nitric acid, more sol in fuming nitric acid. Sparingly sol in hot carbon disulfide and hot carbon tetrachloride. Etches glass slowly.

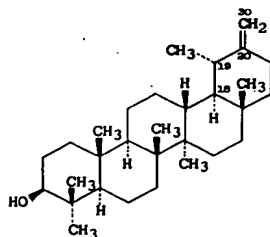
USE: Friedel-Crafts catalyst.

8834. Tantalum Pentoxide. Tantallic acid anhydride. O₅Ta₂; mol wt 441.90. O 18.10%, Ta 81.89%. Ta₂O₅. White, microcryst, infusible powder. Insol in water, alcohol, mineral acids; sol in HF; dec by fusing with KHSO₄ or KOH, forming potassium tantalate with the latter. LD₅₀ orally in rats: > 8.0 g/kg.

8835. Tar Acids. Tar acids are the phenols obtained from coal tar distillates or synthesized from coal tar hydrocarbons. Examples: Phenol, cresol, cresylic acid, xlenol.

8836. Taraxacum. Dandelion; lion's tooth. Dried rhizome and roots of *Taraxacum palustre* (Lyons) Lam. & DC. (*T. officinale* Weber, *Leontodon taraxacum* L.), *Compositae*. *Habit.* Europe; naturalized in North America. *Constit.* Taraxerol, choline, levulin, inulin, pectin.

8837. Taraxasterol. 18α,19α-Urs-20(30)-en-3β-ol; taraxast-20(30)-en-3β-ol; anthesterin; α-lactuceryl; taraxasterin. C₃₀H₅₀O; mol wt 426.70. C 84.44%, H 11.81%, O 3.75%. A monohydroxy triterpene. Isolin from *Taraxacum officinale*, Wiggers, *Compositae*: Power, Browning, *J. Chem. Soc.* 101, 2411 (1912). Structure and configuration: Ames et al., *ibid.* 1954, 1905. Identity with anthesterin: Power, Browning *ibid.* 105, 1829 (1914); with α-lactuceryl: Zellner, *Monatsh.* 47, 681 (1926).



Needles from alcohol, mp 221-222°. [α]_D +96.3° (CHCl₃). Very sol in alcohol, ether, petr ether; slightly sol in chloroform, benzene, carbon disulfide, acetone.

Acetate, C₃₂H₅₂O₂, *lactuceryl*, *lactucon*. Hexagonal plates. mp 251-252° (from ethyl acetate + alcohol). [α]_D +100.5°.

8838. Taraxein. A protein complex isolated from the blood serum of schizophrenics by chromatography on diethylaminoethyl cellulose. The taraxein fraction precedes the ceruloplasmin fraction. Contains copper bound to protein. Method of isolation: Heath et al., *Am. J. Psychiat.* 114, 14 (1957); (*Lippincott's Medical Science* 6, 401 (1959). Processing and identification: Heath et al., *Proc. 3rd World Congr. Psychiat.*, Montreal, 1961 1, 619 (1962). Studies of